Synthesis and Enantiomer Recognition of Novel Crown Ethers containing the 5,6,11,12-Tetrahydro-5,11-methanodibenzo[*a,e*]cyclo-octene Subunit as the Chiral Centre

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The optically active crown ethers (**4**), (**5**), (**7**), (**9**), and (**10**) and the open-chain polyether (**6**), all of which incorporate the 5,6,11,12-tetrahydro-5,11-methanodibenzo[*a,e*]cyclo-octene molecular framework of known absolute configuration, were prepared, and their enantiomer recognition behaviour with methyl (±)-phenylglycinate hydrochloride or (±)-1,2-diphenylethylamine hydrochloride was examined.

A large number of chiral crown ethers have been prepared, and various types of molecule with C_2 symmetry have been employed as the chiral subunit.[1] We now report the synthesis of the chiral crown ethers (**4**), (**5**), (**7**), (**9**), and (**10**) and open-chain polyether (**6**), all of which incorporate the 5,6,11,12-tetrahydro-5,11-methanodibenzo[*a,e*]cyclo-octene molecular framework as the chiral subunit with C_2-symmetry and their enantiomer recognition properties.

We have already reported the preparation of the diketone (**1**) and the glycol (**3**) in optically active forms and the determination of their absolute configuration.[2] The glycol (**8**) possessing hydroxymethyl groups was prepared as follows. Wittig condensation of (−)-(1*S*,5*S*)-(**1**), $[\alpha]_D^{24}$ −325° (EtOH),[2] with methyltriphenylphosphonium bromide using potassium t-butoxide and tetrahydrofuran (THF)[3] gave a 92% yield of (−)-(**2**), m.p. 126—127 °C (from MeOH); $[\alpha]_D^{27}$ −391° (EtOH).[2] Treatment of (−)-(**2**) with diborane in THF[4] led to the corresponding organoborane which was oxidized with 30% H_2O_2 in THF; treatment with 3 M aqueous sodium hydroxide[5] provided (+)-(**8**),† m.p. 170—172 °C (benzene); $[\alpha]_D^{27}$ +143° (EtOH) in 85% overall yield.

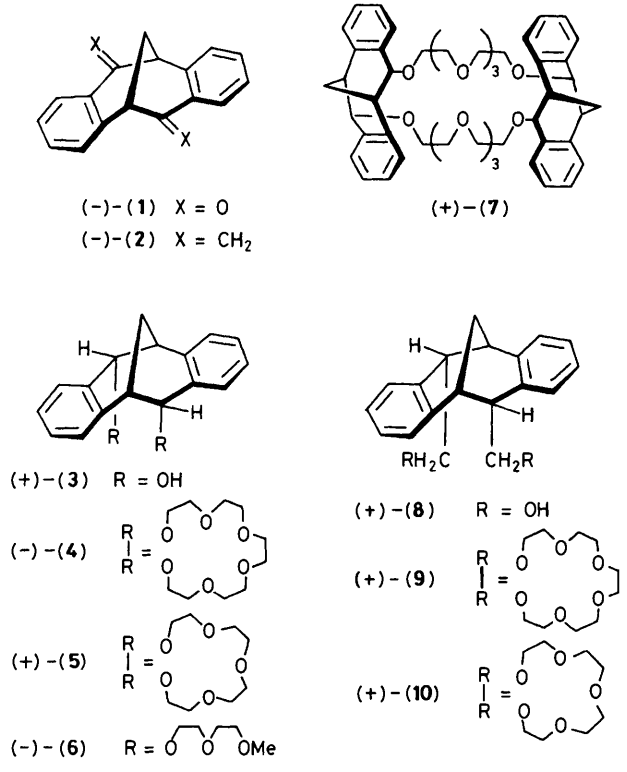
Reaction of (+)-(1*S*,4*R*,5*S*,8*R*)-(**3**), $[\alpha]_D^{24}$ +86.9° (EtOH)[2] with 3,6,9,12-tetraoxatetradecane-1,14-diyl bistoluene-*p*-sulphonate (pentaethyleneglycol ditosylate) in a mixture of NaH and THF (refluxed and stirred under nitrogen for 24 h) afforded (−)-(**4**) in 16% yield after chromatography (Al_2O_3); $CHCl_3$), m.p. 116—117 °C (hexane); $[\alpha]_D^{26}$ −1.5° ($CHCl_3$); ^{1}H n.m.r. ($CDCl_3$), δ 2.20 (t, *J* 3 Hz, CH_2) and 4.67 (d, *J* 4.5 Hz, 2CHO). Condensation of (+)-(**3**) with 3,6,9-

† Satisfactory analytical and spectroscopic data have been obtained for all new compounds.

Table 1. Differential transport[6] of enantiomeric molecules through bulk liquid membranes containing crown ethers and open-chain polyether.[a]

Host[b]	Guest	Time/h	Transport/%	Configuration of dominant enantiomer	Optical purity/%
(−)-(**4**)	[c]	3.5	14	*S*	74
(+)-(**5**)	[c]	4	17	*S*	38
(−)-(**6**)	[c]	1.5	11	*S*	84
(+)-(**7**)	[c]	1.5	12	*S*	53
(+)-(**9**)	[c]	3	14	*S*	32
(+)-(**10**)	[c]	2.5	15	*S*	80
(−)-(**4**)	[d]	48	14	—	0
(+)-(**5**)	[d]	22	26	*R*	23
(−)-(**6**)	[d]	72	15	*S*	8
(+)-(**7**)	[d]	42	11	*R*	5
(+)-(**9**)	[d]	36	12	—	0

[a] Carried out in conventional apparatus (ref. 7) which consisted of an outer cylindrical glass vessel (24.5 mm inner diameter) and a central glass tube (15.5 mm inner diameter). An 0.01 M $CHCl_3$ solution of the host separated the inner (0.1 M HCl) and outer aqueous phases (0.08 M HCl) which contained $LiPF_6$ (0.4 M) and the racemic guest (0.08 M). The organic layer was stirred at a constant speed (60 r.p.m.) at 20 °C, and transport was followed by monitoring the absorbance at 262 nm and $[\theta]_{262}$ of the inner aqueous phase. [b] In the absence of the host, there was no detectable transfer of the substrates. [c] (±)-1,2-Diphenylethylamine hydrochloride. [d] Methyl (±)-phenylglycinate hydrochloride.



trioxaundecane-1,12-diyl bistoluene-*p*-sulphonate (tetraethyleneglycol ditosylate) (NaH–THF) followed by chromatography on alumina gave (+)-(**5**) (11%, eluted with benzene–$CHCl_3$, 9:1), m.p. 72—74 °C (hexane); $[\alpha]_D^{25}$ +42.6° ($CHCl_3$); ^{1}H n.m.r. ($CDCl_3$) δ 2.18 (t, *J* 3 Hz, CH_2) and 5.20 (d, *J* 4.5 Hz, 2CHO), and (+)-(**7**) (12%, eluted with benzene–$CHCl_3$, 8:2), m.p. 167—168 °C (hexane–benzene); $[\alpha]_D^{25}$ +5.4° ($CHCl_3$); ^{1}H n.m.r. ($CDCl_3$) δ 2.12 (t, *J* 3 Hz, $2CH_2$) and 4.63 (d, *J* 4.5 Hz, 4CHO). Treatment of (+)-(**3**) with 6-methoxy-3-oxapentan-1-yl toluene-*p*-sulphonate in a mixture of NaH and *N*,*N*-dimethylformamide (stirred at 45 °C for 24 h) led to the open-chain polyether (−)-(**6**) in 86% yield after chromatography (Al_2O_3; hexane–benzene, 1:1) as a colourless oil, $[\alpha]_D^{20}$ −34.0° ($CHCl_3$); ^{1}H n.m.r. ($CDCl_3$) δ 2.32 (t, *J* 3 Hz, CH_2), 3.36 (s, 2OMe), and 4.74 (d, *J* 4.5 Hz, 2CHO). The glycol (+)-(**8**) was condensed with pentaethyleneglycol ditosylate (NaH–THF) to give (+)-(**9**) in 12% yield after chromatography (Al_2O_3; benzene–$CHCl_3$, 8:2) as a glass, $[\alpha]_D^{23}$ +51.2° ($CHCl_3$); ^{1}H n.m.r. ($CDCl_3$) δ 2.20 (br. s, CH_2). Treatment of (+)-(**8**) with tetraethyleneglycol ditosylate (NaH–THF) followed by chromatography on alumina provided (+)-(**10**) (4%, eluted with benzene–$CHCl_3$, 9:1), $[\alpha]_D^{23}$ +24.0° ($CHCl_3$); ^{1}H n.m.r. ($CDCl_3$) δ 2.15 (br. s, CH_2), as well as the dehydrated product (−)-(**2**) (43%, eluted with benzene).

Table 1 shows the enantiomer recognition behaviour of these polyethers with (±)-1,2-diphenylethylamine hydrochloride and methyl (±)-phenylglycinate hydrochloride. Table 1 shows (a) that all crown ethers that contain the methanodibenzo[*a*,*e*]cyclo-octene molecular framework transport (±)-1,2-diphenylethylamine hydrochloride more rapidly than methyl (±)-phenylglycinate hydrochloride, and have a higher enantiomer selectivity towards (±)-1,2-diphenylethylamine hydrochloride than towards methyl (±)-phenylglycinate hydrochloride, and (b) that the enantiomer selectivity of the open-chain polyether (**6**) is comparable to that of crown ethers (**4**), (**5**), (**7**), (**9**), and (**10**).

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